

'SHARCILLIN'

Crystalline Procaine Penicillin G

For Aqueous Injection

For Intramuscular Use Only

'SHARCILLIN'

FORTIFIED

Crystalline Procaine Penicillin G with

Buffered Crystalline Sodium Penicillin G

For Aqueous Injection

WELLCOME
LIBRARY

P

9373



22502621776

'SHARCILLIN'

Crystalline Procaine Penicillin G

For Aqueous Injection

For Intramuscular Use Only

'Sharcillin' Crystalline Procaine Penicillin G is a sterile powder prepared from the procaine salt of penicillin with dispersing agents added. When the appropriate amount of aqueous diluent is added to the contents of a vial of 'Sharcillin', a free-flowing suspension for intramuscular injection is obtained that provides 300,000 units of crystalline procaine penicillin G per cubic centimeter, with the equivalent of 120 mg. of procaine base.

'Sharcillin' in the dry form is stable at room temperature for eighteen months; refrigeration, therefore, is not necessary. Aqueous suspensions may be stored at room temperature for one week or in the refrigerator for three weeks without significant loss of potency.

Advantages

'Sharcillin' has certain advantages over the commonly employed penicillin preparations:

(1) Following intramuscular injection of an aqueous suspension of 'Sharcillin' the antibiotic is released slowly into the circulatory system, and continuous and prolonged penicillin blood levels are obtained. A single 1 cc. injection (300,000 units) of 'Sharcillin' results in demonstrable penicillin blood levels (0.03 unit or more per cc.) for at least 24 hours in the majority of patients (see table). Excretion in the urine may continue for a considerably longer period of time. Although penicillin in the body may be detected, "demonstrable blood level" does not necessarily mean that penicillin is present in concentrations that are therapeutically effective. Dosage and frequency of administration should be governed by the clinical response of the patient to treatment and the nature of the disease.

(2) The aqueous suspension of 'Sharcillin' is easily administered. The material flows freely in the syringe and needle, and complete absorption in the tissues is obtained. Thus clogging of needles with oily suspensions is obviated, as well as discomfort to the patient because of unabsorbed injected material.

Preparation of Suspension and Method of Administration

(1) Add 1.0 cc. of Water for Injection U.S.P., Dextrose for Injection 5% U.S.P. or Sterile Isotonic Sodium Chloride Solution for Parenteral Use U.S.P. to the one dose vial of 'Sharcillin'. Add 4.5 cc. and 9.0 cc. of sterile diluent, respectively, to the five dose and ten dose vials of 'Sharcillin'. (Insertion of the diluent with the vial in

the inverted position aids in obtaining a uniform suspension.) The suspension in each instance contains 300,000 units of crystalline procaine penicillin G per cubic centimeter.

(2) The suspension of 'Sharcillin' should be at room temperature at the time of injection. Shake well before withdrawing the required dose of penicillin.

Penicillin Blood Levels After Single Intramuscular Injection of 300,000 Units (1 CC.) of 'Sharcillin'

PATIENT No.	UNITS/CC. 24 Hours
1.....	0.10
2.....	0.04
3.....	0.05
4.....	0.20
5.....	0.00
6.....	0.04
7.....	0.12
8.....	0.12
9.....	0.50
10.....	0.04
11.....	0.25
12.....	0.06
13.....	0.12
14.....	0.08
15.....	0.16
16.....	0.16
17.....	0.16
18.....	0.04
19.....	0.10
20.....	0.07

(3) Use a 20 gauge needle for withdrawing and injecting the suspension of 'Sharcillin' and make injection immediately after the suspension has been withdrawn into the syringe.

(4) After inserting needle into chosen site for injection, exert negative pressure by pulling back gently on plunger and observe open end of needle in syringe for evidence of blood, indicating that needle is in a vein. If blood is present a new injection site must be chosen.

(5) Administer slowly by intramuscular injection only. Do not massage injection site.

Clinical Indications and Dosage

'Sharcillin' is indicated in the treatment of infections in which penicillin is indicated, particularly those infections in which prolonged penicillin blood levels are desired. The prolonged effect obtained with this preparation is shortened, however, in ambulatory patients and allowances for this should be made, therefore, when treating individuals who are not at bed rest.

Gonorrhea and Gonococcic Infections

Single injection of 300,000 units (1 cc.) is sufficient for most cases of acute gonorrhea. In cases of failure, treatment may be repeated until cure is effected. In chronic cases, and those complicated by arthritis, epididymitis and salpingitis, intensified and prolonged treatment is required.

If a suspected primary lesion of syphilis is present, dark field examinations should be made before starting penicillin therapy. In all other cases in which concomitant syphilis is suspected, monthly serologic tests should be made for at least three months.

Pneumonia and Other Acute Pneumococcic, Staphylococcic and Streptococcic Infections

A minimum of 300,000 units (1 cc.) of 'Shar-cillin' every 24 hours until 48 hours after the temperature has returned to normal usually is sufficient. In severe infections from 300,000 to 600,000 units (1 to 2 cc.) should be administered every 12 to 24 hours.

Primary and Secondary Syphilis

A minimum of 600,000 units (2 cc.) of 'Shar-cillin' daily for 10 days is suggested. This dosage schedule is only tentative and is subject to change as further information on penicillin therapy in syphilis is accumulated. It is of great importance to carry out frequent serologic and clinical examinations in all patients during the post-treatment period when penicillin therapy is employed, i.e., every month for the first twelve months and then every six months for at least two to three years.

In treating relapses of syphilis the dosage schedules recommended by the Syphilis Study Section, National Institute of Health, should be followed.¹

Meningitis

Dosage schedules for the treatment of meningitis with procaine penicillin have not been established as yet. At present it is suggested that sulfonamide therapy and/or aqueous solution of penicillin be employed.

Bacterial Endocarditis

Aqueous solution of penicillin is recommended in a dosage of 500,000 to 2,000,000 units or more daily for from 6 to 8 weeks or longer. In cases that respond favorably 'Sharcillin' may be administered as supplemental therapy after the infection is under control, in a dosage of 600,000 units (2 cc.) every 12 hours.

Miscellaneous

From 300,000 to 600,000 units (1 to 2 cc.) of 'Sharcillin' once or twice daily is recommended in the treatment of Vincent's infection, erysiploid (swine erysipelas), anthrax, and for the prevention of secondary infection following tonsillectomy and tooth extraction in cases of rheumatic fever or in rheumatic or congenital heart disease or in other cases in which secondary infections are likely to occur (infected teeth or tonsils).

'Sharcillin' also may be employed for the treatment of spirochetal diseases. It may be used in the treatment of diphtheria and scarlet fever with concomitant administration of specific antitoxin.

The optimal dosage of 'Sharcillin' for infants and children has not yet been determined. As much as 150,000 units ($\frac{1}{2}$ cc.) every 24 hours is suggested for infants in treatment of most acute infections due to penicillin-sensitive organisms.

Precautions

'Sharcillin' should not be injected intravenously or subcutaneously.

Allergic reactions probably will occur in patients allergic to penicillin or to procaine. In the presence of hypersensitivity reactions such as urticaria, angioneurotic edema and the like, it may be necessary to discontinue administration of this preparation, unless symptoms can be controlled with appropriate agents, or unless the severity of the infection makes continuation of the drug imperative in spite of the reaction. Treatment with another type of penicillin preparation may prove to be satisfactory.

Each cubic centimeter of 'Sharcillin' contains the equivalent of 120 mg. of procaine base. Considerably greater amounts of procaine have been administered intravenously by various investigators.²⁻⁵ Since absorption of procaine penicillin G into the blood stream is slow, toxic levels of procaine probably will not be attained following the intramuscular injection of recommended doses.

An intradermal procaine test, using 0.1 cc. of a 1 or 2 per cent solution of procaine, should be performed if sensitivity to this substance is suspected. In the presence of a positive reaction this type of penicillin preparation should not be administered.

How Supplied

'Sharcillin' Crystalline Procaine Penicillin G is supplied as follows:

One dose vials.....300,000 units of penicillin
Five dose vials1,500,000 units of penicillin
Ten dose vials3,000,000 units of penicillin

References

1. Syphilis Study Section, National Institute of Health, U. S. Public Health Service, J.A.M.A. 136:873, March 27, 1948.
2. Graubard, D. J., Robertazzi, R. W., and Peterson, M. C., New York State J. Med. 47:2187, Oct. 15, 1947.
3. Graubard, D. J., and Ritter, H. H., Am. J. Surg. 74:765, Nov. 1947.
4. State, D., and Wangenstein, O. H., J.A.M.A. 130:990, April 13, 1946.
5. Burstein, C., Anesthesiology 7:113, March 1946.

'SHARCILLIN' FORTIFIED

*Crystalline Procaine Penicillin G with
Buffered Crystalline Sodium Penicillin G
for Aqueous Injection*

For Intramuscular Use Only

'Sharcillin' Fortified is a mixture of the crystalline procaine and sodium salts of penicillin with dispersing agents added. When the appropriate amount of aqueous diluent is added to the contents of a vial of 'Sharcillin' Fortified, a free-flowing suspension for intramuscular injection is obtained that provides 300,000 units of crystalline procaine penicillin G and 100,000 units of buffered crystalline sodium penicillin G per cubic centimeter, with the equivalent of 120 mg. of procaine base.

'Sharcillin' Fortified in the dry form is stable at room temperature for eighteen months; refrigeration, therefore, is not necessary. Aqueous suspensions may be stored at refrigerator temperatures for one week without significant loss of potency.

Advantages

'Sharcillin' Fortified has certain advantages over the commonly employed penicillin preparations:

(1) Following intramuscular injection of an aqueous suspension of 'Sharcillin' Fortified, high penicillin blood levels are attained promptly, which frequently are necessary in treatment of acute and chronic infections. These high concentrations are due to the presence of *sodium penicillin* in aqueous *solution*, which is absorbed rapidly into the blood stream. A maintenance level then is provided for 24 hours in almost all patients, owing to the slow release of *procaine penicillin* in aqueous *suspension*. The combination of sodium and procaine salts of penicillin in 'Sharcillin' Fortified thus maintains high penicillin concentrations during the early hours after injection and demonstrable levels (0.03 unit or more per cc.) for a prolonged period.

A single 1 cc. injection (400,000 units) of 'Sharcillin' Fortified results in penicillin blood levels of 2.5 units/cc. or more in almost all patients during the one to three hour period following administration, and demonstrable levels are present at 24 hours (see table). Although penicillin in the body may be detected, "demonstrable blood level" does not necessarily mean that penicillin is present in concentrations that are therapeutically effective. Dosage and frequency of administration should be governed by the clinical response of the patient to treatment and the nature of the disease.

(2) The aqueous solution-suspension of 'Sharcillin' Fortified is easily administered. The material flows freely in the syringe and needle, and complete absorption in the tissues is obtained. Thus clogging of needles with oily suspensions is obviated, as well as discomfort to the patient because of unabsorbed injected material.

Preparation of Suspension and Method of Administration

(1) Add 1.0 cc. of Water for Injection U.S.P., Dextrose for Injection 5% U.S.P. or Sterile Isotonic Sodium Chloride Solution for Parenteral Use U.S.P. to the one dose vial of 'Sharcillin' Fortified. Add 4.5 cc. and 9.0 cc. of sterile dilu-

Penicillin Blood Levels After Single Intramuscular Injection of 400,000 Units (1 CC.) of 'Sharcillin' Fortified*

PATIENT No.	UNITS/CC.		
	<i>1 Hour</i>	<i>2 Hours</i>	<i>24 Hours</i>
1	2.50	1.25	0.04
2	2.50	1.25	0.04
3	2.80	2.50	0.08
4	1.25	1.25	0.04
5	2.50	1.25	0.04
6	1.25	1.25	0.04
7	0.63	0.63	0.08
8	2.50	2.50	0.04
9	2.50	2.50	0.04
10	3.00	2.50	0.08
11	3.96	3.96	0.08
12	2.50	2.50	0.00
13	2.50	2.50	
14	2.50	1.25	0.08
15	2.50	2.50	0.08

*These patients were at bed rest. In ambulatory patients levels may not be so prolonged. Detectable penicillin levels may be present in the urine for periods longer than 24 hours.

ent, respectively, to the five dose and ten dose vials of 'Sharcillin' Fortified. (Insertion of the diluent with the vial in the inverted position aids in obtaining a uniform suspension.) The suspension in each instance contains 400,000 units of penicillin per cubic centimeter (300,000 units of crystalline procaine penicillin G and 100,000 units of buffered crystalline sodium penicillin G).

(2) The suspension of 'Sharcillin' Fortified should be at room temperature at the time of injection. Shake well before withdrawing the required dose of penicillin.

(3) Use a 20 gauge needle for withdrawing and injecting the suspension of 'Sharcillin' Fortified and make injection immediately after the suspension has been withdrawn into the syringe.

(4) After inserting needle into chosen site for injection, exert negative pressure by pulling back gently on plunger and observe open end of needle in syringe for evidence of blood, indicating that needle is in a vein. If blood is present a new injection site must be chosen.

(5) Administer slowly by intramuscular injection only. Do not massage injection site.

Clinical Indications and Dosage

'Sharcillin' Fortified is indicated in the treatment of infections in which penicillin is indicated, particularly those infections in which high initial penicillin blood levels as well as prolonged maintenance levels are desired. The prolonged effect obtained with this preparation is shortened, how-

ever, in ambulatory patients and allowances for this should be made, therefore, when treating individuals who are not at bed rest.

Gonorrhea and Gonococcic Infections

Single injection of 400,000 units (1 cc.) is sufficient for most cases of acute gonorrhea. In cases of failure, treatment may be repeated until cure is effected. In chronic cases, and those complicated by arthritis, epididymitis and salpingitis, intensified and prolonged treatment is required.

If a suspected primary lesion of syphilis is present, dark field examinations should be made before starting penicillin therapy. In all other cases in which concomitant syphilis is suspected, monthly serologic tests should be made for at least three months.

Pneumonia and Other Acute Pneumococcic, Staphylococcic and Streptococcic Infections

A minimum of 400,000 units (1 cc.) of 'Sarcillin' Fortified every 24 hours until 48 hours after the temperature has returned to normal usually is sufficient. In severe infections from 400,000 to 800,000 units (1 to 2 cc.) should be administered every 12 to 24 hours.

Primary and Secondary Syphilis

A minimum of 800,000 units (2 cc.) of 'Sarcillin' Fortified daily for 10 days is suggested. This dosage schedule is only tentative and is subject to change as further information on penicil-

lin therapy in syphilis is accumulated. It is of great importance to carry out frequent serologic and clinical examinations in all patients during the post-treatment period when penicillin therapy is employed, i.e., every month for the first twelve months and then every six months for at least two to three years.

In treating relapses of syphilis the dosage schedules recommended by the Syphilis Study Section, National Institute of Health, should be followed.¹

Meningitis

Dosage schedules for the treatment of meningitis with procaine penicillin and sodium penicillin have not been established as yet. At present it is suggested that sulfonamide therapy and/or aqueous solution of penicillin be employed.

Bacterial Endocarditis

Aqueous solution of penicillin is recommended in a dosage of 500,000 to 2,000,000 units or more daily for from 6 to 8 weeks or longer. In cases that respond favorably 'Sharcillin' Fortified may be administered as supplemental therapy after the infection is under control, in a dosage of 800,000 units (2 cc.) every 12 hours.

Miscellaneous

From 400,000 to 800,000 units (1 to 2 cc.) of 'Sharcillin' Fortified once or twice daily is recommended in the treatment of Vincent's infection, erysipeloid (swine erysipelas), anthrax, and for the prevention of secondary infection

following tonsillectomy and tooth extraction in cases of rheumatic fever or in rheumatic or congenital heart disease or in other cases in which secondary infections are likely to occur (infected teeth or tonsils).

'Sharcillin' Fortified also may be employed for the treatment of spirochetal diseases. It may be used in the treatment of diphtheria and scarlet fever with concomitant administration of specific antitoxin.

The optimal dosage of 'Sharcillin' Fortified for infants and children has not yet been determined. As much as 200,000 units ($\frac{1}{2}$ cc.) every 24 hours is suggested for infants in treatment of most acute infections due to penicillin-sensitive organisms.

Precautions

'Sharcillin' Fortified should not be injected intravenously or subcutaneously.

Allergic reactions probably will occur in patients allergic to penicillin or to procaine. In the presence of hypersensitivity reactions such as urticaria, angioneurotic edema and the like, it may be necessary to discontinue administration of this preparation, unless symptoms can be controlled with appropriate agents, or unless the severity of the infection makes continuation of the drug imperative in spite of the reaction. Treatment with another type of penicillin preparation may prove to be satisfactory.

Each cubic centimeter of 'Sharcillin' Fortified contains the equivalent of 120 mg. of procaine base. Considerably greater amounts of procaine

have been administered intravenously by various investigators.²⁻⁵ Since absorption of procaine penicillin G into the blood stream is slow, toxic levels of procaine probably will not be attained following the intramuscular injection of recommended doses.

An intradermal procaine test, using 0.1 cc. of a 1 or 2 per cent solution of procaine, should be performed if sensitivity to this substance is suspected. In the presence of a positive reaction this type of penicillin preparation should not be administered.

How Supplied

'Sharcillin' Fortified Crystalline Procaine Penicillin G with Buffered Crystalline Sodium Penicillin G is supplied as follows:

One dose vials400,000 units of penicillin
Five dose vials2,000,000 units of penicillin
Ten dose vials4,000,000 units of penicillin

References

1. Syphilis Study Section, National Institute of Health, U. S. Public Health Service, J.A.M.A. 136:873, March 27, 1948.
2. Graubard, D. J., Robertazzi, R. W., and Peterson, M. C., New York State J. Med. 47:2187, Oct. 15, 1947.
3. Graubard, D. J., and Ritter, H. H., Am. J. Surg. 74:765, Nov. 1947.
4. State, D., and Wangenstein, O. H., J.A.M.A. 130:990, April 13, 1946.
5. Burstein, C., Anesthesiology 7:113, March 1946.

SHARP & DOHME

PHARMACEUTICALS • BIOLOGICALS

Philadelphia 1, Pa.